as those of the Cancer Data Standards Registry and Repository (caDSR) need to be adopted more widely to ensure uniformity. For a given biomarker, a classification needs to include the type of marker (whether diagnostic, prognostic, predictive, or companion diagnostic), the marker's characteristics (e.g. what it is measuring in terms of pathways, or receptor status, at the molecular level), the physiologic compartment source (e.g. blood, urine, tissue, CSF, bone marrow), and the setting including clinical presentation and scenario specificity (i.e. when the marker is useful and relevant). For the latter the decision will also need to address whether new diseases (e.g. HPV-driven cancer) should continue to be combined with the classic version of oropharyngeal cancer since emerging data has underlined the separate nature of these processes at the etiology, clinical, pathological, molecular, and outcome levels. This may also extend to whether the TNM classification should even be the same for both diseases.

SP-0102
Redefining the dose distribution (i.e. dose painting with/without dose escalation/dose de-escalation)
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In the near future rational individualisation of radiation dose prescription will be possible. Current technology now allows the distribution of radiation dose to be tightly controlled and advances in our understanding of the biology of the disease will lead to individualisation of radiation dose delivery both within individual patients and between different patients.
Functional imaging is at the present time the most likely candidate technology to influence our choice of individualising the dose distribution, however a number of unanswered questions remain before this can become a reality.
This presentation will review the current state of this area of research and discuss likely forward directions of research. Clinical trials to evaluate these technologies will be discussed.

SP-0103
Defining the need for systemic treatment, e.g. which agents and when.
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Abstract not received

JOINT SYMPOSIUM: ESTRO-RANZCR: MANAGEMENT OF LIVER OLIGO-METASTATIC DISEASE

SP-0104
Radiofrequency ablation for liver metastases
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Radiofrequency ablation (RFA) is regarded as the primary ablative modality for local tumour destruction at most institutes. It involves delivery of high-frequency, in the range of 375 to 500 kHz, alternating electrical current into the target tissue through a needle electrode. Electrical current passes back and forth through the body between the electrode and some grounding pads putting on the skin of the thighs. The high frequency of alternating current causes rapid movement of the ions or charged molecules within the cells in the tissue surrounding the electrode. Heat is produced by friction during the rapid movement of these molecules. Temperature in excess of 50 °C produces coagulative necrosis. A 2 to 5 cm spherical thermal injury can be produced with each ablation, depending on the design of the needle electrode.
The main aim of thermal tumour ablation therapy is to destroy an entire tumour, with a 1 cm margin, in a minimally invasive fashion without damaging adjacent vital structures. Each ablation requires exact placement of electrode in the tumour. Any radiofrequency needle electrodes can be inserted percutaneously, under laparoscopic guidance or during laparotomy. With percutaneous approach, the electrodes can be placed under sonographic, CT, or MR guidance.
The major complications associated with RFA occur in 2.2–3.1% of patients. The minor complication rate ranges from 5% to 8.9%. Complications are divided into 3 different types: thermal damage (gastrointestinal perforation, biliary stenosis, cardiac tamponade and grounding pad burns), mechanical complications (injuries to bile ducts and vessels, tumour seeding and hemorrhage), and septic complications (abscess and peritonitis). Treatment of lesions adjacent (< 1 cm) to the hepatic hilum increases the risk of thermal injury of the major biliary tract and represents a relative contraindication to RFA. Thermal ablation of lesions adjacent to hepatic vessels increases the risk of incomplete treatment of the neoplastic tissue close to the vessel due to heat loss or heat sink effect.
From the recent data on long-term survival of nonsurgical patients (due to comorbidity, patient refusal or unfavourable anatomy) with colorectal liver metastases (CRLM) who underwent RFA, the 5-year survival rate ranges 24–44%. These figures are substantially higher than those obtained with any chemotherapy regimens and provide indirect evidence that RFA therapy improves survival in patients with limited hepatic metastatic disease.
Currently, liver resection (LR) is regarded as the gold standard treatment for resectable CRLM. One of the greatest criticisms for the utilization of RFA for treatment of CRLM has been a concern of high local recurrence at the RFA site. Local recurrence rates after RFA in the literature have been quite variable and range from 4% to 55%. A recent meta-analysis found the overall local recurrence rate to be 14.7%.
Multiple studies have been published comparing RFA to LR for treatment of CRLM. In a recent published meta-analysis, 3-year and 5-year disease free survival as well as 3- year and 5-year overall survival are significantly higher in the LR group.
Based on these retrospective reports, several authors have concluded that RFA is not equivalent to surgical resection and therefore should not be used to treat lesions that are otherwise resectable. Due to the retrospective nature of these studies, and the significant bias in patient selection, these results are difficult to interpret and the role of RFA remains biased. In addition, these retrospective studies are not randomized.
The use of RFA does not prevent simultaneous or subsequent use of other, potentially complementary, treatments. Combining with other treatment modality is probably the future direction for RFA in the treatment of CRLM.
There is limited data on the use of RFA in treating hepatic metastases from non CRLM. The conclusion from those published studies employing RFA to treat non CRLM is that RFA is regarded as an adjunct to resection and unresectable lesions that demonstrate positive response after chemotherapy.

SP-0105
Radiotherapy for liver metastases
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The present evidence for local ablation of liver oligo-metastases is limited. No randomized controlled trial has ever proven the efficacy of local ablation on survival, and the evidence is even poorer when it comes to comparisons of the different ablation methods. Surgical resection has by tradition been the preferred therapy for liver oligo-metastases and radiofrequency ablation (RFA) is frequently used for treatment of inoperable patients. Stereotactic body radiation therapy (SBRT) is most often number three in line and has been used for therapy of medical inoperable patients and patients who are not amendable for surgery or RFA for technical reasons. These reasons are most often related to size of the metastases or the anatomical distribution in the liver. Where SBRT has been standard of care in therapy of patients with limited stage non-small cell cancer and lungmetastases for some time, the introduction of SBRT in the treatment of tumors in the liver has been characterized by hesitation.
A number of retrospective and few prospective studies have been published on SBRT for liver metastases. In general, studies are characterized by considerably heterogeneity concerning patient selection. Retrospective studies often include a variety of tumor types with variability of number and size of the metastases and this translates into a broad variability in outcome. The most frequent tumor type investigated is colorectal carcinoma (CRC) metastases, but there are studies including almost all tumor types. Some studies show that survival outcomes are not different for CRC and non-CRC patients. Most studies demonstrate high local control rates ranging 80-90% in SBRT for liver metastases. Treatment techniques, doses and fractionation varies between the studies, but an effect of dose escalation on the local control is fairly consistent. It is generally accepted that when using a 3 fraction schedule, the prescription dose should be at least 48 Gy.
The morbidity after SBRT for liver metastases is mild to moderate. Most often it is limited to temporary abdominal wall pain, rib fracture and erythema. Severe morbidity related to exposure of the stomach or bowel and hepatic failure due to radiation hepatitis, a few being fatal, have been reported.
Novel radiotherapy techniques have contributed to the improved precision in delivery of largeradiation doses to defined targets by

SBRT. Multimodal imaging for target definition, image guidance techniques utilizing implanted fiducial markers, 4D-CT scanning and respiration management techniques have considerable improved the SBRT.
In general, the approach to metastatic disease has become more aggressive. A number of specialties offer therapies for patients with liver oligo-metastases and a multidisciplinary team approach in the management of these patients is of utmost importance. Radiotherapy may be utilized for a group of patients who cannot be treated by surgery or RFA and the radiation oncologist should therefore be a member of the team.
There is sufficient data demonstration that SBRT can be used in therapy of liver metastases when the constraints to critical tissues such as stomach, bowel and lover are respected, but there is a great need for randomized clinical trials to prove the efficacy of SBRT in treatment of oligo-metastases and for trials to explore the need for systemic therapy along with SBRT. It is therefore strongly encouraged to participate in large multi-institutional randomized trials.

SP-0106
The role of surgical resection in liver oligo-metastatic disease
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When a patient is diagnosed with liver metastases it is by definition a systemic disease and metastases at other sites should also be expected. This is also the case for the third most common cancer disease, colorectal cancer (CRC). Almost half of all patients with CRC will develop liver metastases (CLM) and approximately a fourth of them have only the liver as metastatic site. If the patient has no serious co-morbidities and 30 percent of the liver parenchyma and one hepatic vein can be saved there is indication for liver resection. This is a relative safe procedure with a postoperative mortality below five percent and this subpopulation of patients with CRC has a 5-year survival of 40-50 percent and 30 percent 10-year survival.
The good outcome in liver resected patients is the main reason for follow-up with tumour markers and CT scan after surgery of the primary tumour.
Neoadjuvant chemotherapy will slightly improve progression free survival but not overall survival. Still most patients are today offered neoadjuvant therapy. From a multidisciplinary perspective conversion therapy is important. A majority of patients with CLM will get a response on chemotherapy and they shall then be reconsidered for liver resection. The 5-year survival is as good as for patients who were primarily resectable. On the other hand, patients with CLM that progress on chemotherapy have a bad prognosis, even after liver resection.
From a surgical point of view a patient might have a limited metastatic volume in the liver but one or more small metastases can be badly situated. In this case ablative techniques (radiofrequence or microwave ablation) or stereotactic radiotherapy can be of great value to complement resection of other parts of the liver.
Even if CLM is the most common indication for liver resection of metastatic disease there are other cancer diseases where surgery for oligo-metastatic disease shall be considered. These are primarily neuroendocrine tumours (NET), renal cell cancer, melanoma and ovarian cancer. As with CLM there are no randomised studies to support the indication for surgery but the evidence are generated by comparing survival of liver resected patients with a cohort who had similar tumour burden but were not operated.

SYMPOSIUM: FUNCTIONAL IMAGING FOR RADIO-THERAPY DOSE PAINTING

SP-0107
Quantitative MR imaging for radiotherapy
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Quantitative MRI holds the promise to augment radiotherapy with functional imaging, which may enable improved tumor targeting, and more personalized treatment based on a priori characterization of imaging biomarkers and early assessment of treatment response. This lecture emphasizes some factors of quality, validation, and applications of quantitative MRI metrics.
Diffusion-weighted imaging (DWI) geometric accuracy at 3 Tesla: Geometric accuracy is of fundamental importance for incorporation of anatomic imaging into radiation therapy, yet the geometric accuracy of clinical DWI pulse sequences is under-emphasized. Segmented echo-planar (EPI) DW imaging is an accessible solution on many pre-clinical high-field MRI systems, providing dramatic geometric accuracy improvement compared to single-shot EPI-DWI at similar scan time and signal-to-noise. Utilizing the RESOLVE works-in-progress package provided by Siemens Medical Systems, segmented EPI DWI has been investigated as an option for more geometrically accurate clinical DWI at 3T. The geometric accuracy improvement from RESOLVE is verified using an in vitro prostate phantom, and applied in vivo to enable tumor-targeted radiation therapy treatment planning for prostate cancer at 3 Tesla based on DWI and T_2-weighted image co-registration (see Figure).
Dynamic contrast enhanced (DCE) MRI validation against DCE-CT: DCE-MRI has broad appeal as a clinical biomarker for radiation oncology, yet presents with known limitations to accuracy and precision. These known limitations apply to both vessel-based measurements of arterial input function (AIF) and tumor-based measurements of permeability and perfusion. Methodologic improvements have been incorporated at 3 Tesla and tested against the standard of DCE-CT. First, a multi-modal DCE-MRI/CT flow phantom has been applied to investigate factors affecting AIFs measured using the MRI magnitude signal, and to validate AIFs measured using the MRI signal phase. Second, a 4D temporal segmentation (TDS) method, which enables voxel-based, parametric analysis based on patient-specific dynamic behaviour of contrast flow, has been implemented to facilitate tissue-level analysis. Preliminary testing has compared DCE-CT supported by 4D-TDS to standard DCE-MRI analysis for the detection of early changes in brain tumor perfusion following radiosurgery.
Stromal imaging: Hedgehog (Hh) pathway inhibition is a potential strategy to overcome treatment resistance and repopulation in patients undergoing radiotherapy and concurrent chemotherapy, and it is now widely held that the Hh pathway promotes tumor growth indirectly through paracrine effects on the stroma. MRI biomarkers to monitor Hh inhibition and stromal depletion have been investigated in murine models of human cervical, pancreatic, and breast cancer, utilizing the 7 Tesla MRI of the STTARR facility, with emphasis on DCE-MRI, magnetization transfer, and DWI.
Figure: A prostate DWI geometric distortion phantom, consisting of distilled water within concentric acrylic cylinders of 3, 6, and 12 cm (e.g. corresponding to the outer diameter of the Hologic endorectal coil diameter; the anterior peripheral zone; and the anterior prostate) was imaged with RESOLVE and standard DWI at 3 T (1.4x.1.4x3-mm resolution, 28 slices). (a, b) Meshes of cylinder boundaries for RESOLVE and standard DWI were generated, and cylinder boundaries were tracked to quantify vertical distortion in the phase encoding direction. Compared to standard DWI, RESOLVE reduced the mean RMS displacement of inner and middle cylinders 3-fold (to 0.5 mm) and reduced the maximum distortion in y from 13 to 3 mm. (c-d) clinical prostate RESOLVE and standard DWI ADC maps at 3T in matched slices, verifying distortion reduction in vivo in approximately equivalent scan times and matched spatial resolution (1.4x1.4x3-mm voxels).